SCIT: effective dose

There are very few dose-finding double-blind placebo controlled trials in which several doses are used, as was recently reviewed by a special Task Force of the EAACI.¹

AAAII Practice parameters, 3rd update, recommendations,² see table below.

<table>
<thead>
<tr>
<th>Allergenic extract</th>
<th>Labeled potency or concentration</th>
<th>Probable effective dose range</th>
<th>Range of estimated major allergen content in US-licensed extracts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dust mites: <em>D. farinae</em> and <em>D. pteronyssinus</em></td>
<td>3,000, 5,000, 10,000. and 30,000 AU/mL.</td>
<td>500-2,000 AU</td>
<td>10,000 AU/mL. 20-160 µg/mL. Der p 1, Der f 1⁺ 2-180 µg/mL. Der p 2, Der f 2⁺ 78-206 µg/mL. Der p 1, Der f 1⁺ 13-147 µg/mL. Der p 2, Der f 2⁺</td>
</tr>
<tr>
<td>Cat hair</td>
<td>5,000 and 10,000 BAU/mL.</td>
<td>1,000-4,000 BAU</td>
<td>10,000 BAU/mL. 20-50 µg/mL. Fel d 1⁺ 30-100 µg/mL. cat albumin.</td>
</tr>
<tr>
<td>Cat pelt</td>
<td>5,000-10,000 BAU/mL.</td>
<td>1,000-4,000 BAU</td>
<td>10,000 BAU/mL. 20-50 µg/mL. Fel d 1⁺ 400-2,000 µg/mL. cat albumin.</td>
</tr>
<tr>
<td>Grass, standardized</td>
<td>100,000 BAU/mL.</td>
<td>1,000-4,000 BAU</td>
<td>100,000 BAU/mL. 425-1,100 µg/mL. Phl p 5⁺ 506-2,346 µg/mL. group I.</td>
</tr>
<tr>
<td>Bermuda</td>
<td>10,000 BAU/mL.</td>
<td>300-1,500 BAU</td>
<td>10,000 BAU/mL. 141-422 Cyn d 1 µg/mL.²</td>
</tr>
<tr>
<td>Short ragweed</td>
<td>1:10, 1:20 w/vol, 100,000 AU/mL.</td>
<td>6-12 µg of Amb a 1 or 1,000-4,000 AU.</td>
<td>1:10 w/vol. 300 µg/mL. Amb a 1 is on the label of w/vol extracts.</td>
</tr>
<tr>
<td>Nonstandardized AP Dog</td>
<td>1:100 w/vol</td>
<td>15 µg of Can f 1</td>
<td>80-400 µg/mL. Can f 1⁺ 10-20 µg/mL. dog albumin.²</td>
</tr>
<tr>
<td>Nonstandardized extract, dog</td>
<td>1:10 and 1:20 w/vol</td>
<td>15 µg of Can f 1</td>
<td>0.5 to 19 µg/mL. Can f 1⁺ &lt;12-1,500 µg/mL. dog albumin.²</td>
</tr>
<tr>
<td>Nonstandardized extracts: pollen</td>
<td>1:10 to 1:40 w/vol or 10,000-40,000 PSU/mL.</td>
<td>0.5 mL of 1:100 or 1:200 w/vol</td>
<td>NA</td>
</tr>
<tr>
<td>Nonstandardized extracts: mold/traumatic, cockroach</td>
<td>1:10 to 1:40 w/vol or 10,000-40,000 PSU/mL.</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Hymenoptera venom</td>
<td>100 µg/mL single venom 300 µg/mL in mixed vespid extract</td>
<td>50-200 µg of each venom</td>
<td>100-300 µg/mL. venom protein.</td>
</tr>
<tr>
<td>Imported fire ant</td>
<td>1:10 to 1:20 w/vol whole-body extract</td>
<td>0.5 mL of a 1:100 w/vol to 0.5 mL of a 1:10 w/vol extract</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA. Information not available.

¹ALK-Abello ELISA.
²Hollister-Stier ELISA using Innovative Research, Inc. reagents.

Practice Parameters state that: ‘it is possible (and supported by expert opinion) that therapeutic response can occur with doses lower than those that have been shown to be effective in controlled studies.’

AND
Although administration of a higher maintenance dose of immunotherapy increases the likelihood of clinical effectiveness, it also increases the risk of systemic reactions. In particular, highly sensitive patients might be at increased risk of a systemic reaction to immunotherapy injections with higher maintenance doses.

**Pollen: grass:** US studies are from the 80ies with extracts standardized in w/vol or PNU. The package inserts for US-licensed grass pollen extracts contain a table to convert the non-standardized units (wt/vol and PNU) for which there have been studies that have demonstrated efficacy into BAUs. Appropriate dose reductions would need to be made when combining antigens that have a strong degree of cross-reactivity, such as the Northern pasture grasses (subfamily Pooidaeae; eg, perennial rye, meadow fescue, or timothy).

**Bermuda grass:** Bermuda grass has an assigned potency of 10,000 BAU, which is 10-fold less than the other standardized grasses.

**Pollen: Ragweed.** Good dose-response US studies, with improvement in nasal challenge end-point.

**Pollen: trees.** No studies. Non-standardized. A target dose of 0.5 mL of a 1:100 or 1:200 wt/vol of nonstandardized extract is reasonable

**HDM:** reference values are exclusively from European studies done end-90ies with aqueous or with aluminum hydroxide polymerized depot extracts given every 6 weeks at maintenance.

1. Depot preparation
2. Interval is different
3. Mite composition is different\(^3\): Der p 1 vs. Der p 2 content. Measuring Der p 1 mcg/ml to ‘convert’ into US equivalent product is not appropriate.

**Alternaria:** recent studies with European ALOH depot products 8mcg Alt a 1 every 4-6 wks showed good efficacy in a high-quality study\(^4\), 0.1mcg\(^5\) and 0.2mcg\(^6\) Alt a 1 every 4wks were less effective.

**SLIT: effective dose**

**Pollen: grass.** US studies very recently conducted with tablets\(^7,8\) and liquid formulations.\(^9\)

**Pollen: Ragweed.** US studies very recently conducted with liquid formulations.\(^9\)

**Pollen: trees.** No US trials

**HDM:** liquid formulation preliminary trial has been done.\(^10\)

**Alternaria.** No US trials.

**Multiple allergen SLIT:** Amar et al (Nelson-group) showed a timothy extract, as part of a 10-allergen mix is probably much less effective as the same timothy dose alone in an extract.\(^11\) A post-hoc analysis of pooled data from several trials showed mono-Timothy grass tablet SLIT is effective in poly-sensitized patients.\(^12\) Very recently Swamy et al. demonstrated the efficacy of glycerinated dual-grass pollen+HDM SLIT in US population.\(^13\)

**Dosing with European SLIT products:** many trials have been conducted of varying quality. There exist marked differences in dosing among the major European allergen manufacturers in SLIT maintenance dose.\(^7\) One study compared their potency against US concentrated extracts with several in vitro tests.\(^3\) Other studies compared skin prick test solution potencies between US and Europe.\(^14,15\) European regulatory authorities are becoming more strict in evaluation of trials needed for registration of IT products.
**Important issues**

How to mix and maintain adequate dose.\(^\text{16}\)

Which extracts can and cannot be mixed.\(^\text{17}\)

What doses are actually used by American Allergists?\(^\text{18}\)

**References**


Note: authorization has been asked to add PDF files to hand-out CD of references 2, 14 and 15.